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| SERIAL NUMBER | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. |
|---|---|---|---|
| 07/565,673 | 08/10/90 | VAN DER LAAN J | 34363/GNRO-0 |

EXAMINER
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18M1

| ART UNIT | PAPER NUMBER |
|---|---|
| 1814 | 15 |

DATE MAILED: 03/02/93

This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

☒ This application has been examined ☒ Responsive to communication filed on 12-15-92 ☒ This action is made final.

A shortened statutory period for response to this action is set to expire 3 month(s), ~~days~~ from the date of this letter.
Failure to respond within the period for response will cause the application to become abandoned. 35 U.S.C. 133

**Part I THE FOLLOWING ATTACHMENT(S) ARE PART OF THIS ACTION:**

1. ☐ Notice of References Cited by Examiner, PTO-892.
2. ☐ Notice re Patent Drawing, PTO-948.
3. ☐ Notice of Art Cited by Applicant, PTO-1449.
4. ☐ Notice of Informal Patent Application, Form PTO-152
5. ☐ Information on How to Effect Drawing Changes, PTO-1474.
6. ☐ _____.

**Part II SUMMARY OF ACTION**

1. ☒ Claims 4-7, 9-17, 19 & 23-26 are pending in the application.
   Of the above, claims _____ are withdrawn from consideration.
2. ☐ Claims _____ have been cancelled.
3. ☐ Claims _____ are allowed.
4. ☒ Claims 4-7, 9-17, 19, & 23-26 are rejected.
5. ☐ Claims _____ are objected to.
6. ☐ Claims _____ are subject to restriction or election requirement.
7. ☒ This application has been filed with informal drawings under 37 C.F.R. 1.85 which are acceptable for examination purposes.
8. ☐ Formal drawings are required in response to this Office action.
9. ☐ The corrected or substitute drawings have been received on _____. Under 37 C.F.R. 1.84 these drawings are ☐ acceptable; ☐ not acceptable (see explanation or Notice re Patent Drawing, PTO-948).
10. ☐ The proposed additional or substitute sheet(s) of drawings, filed on _____. has (have) been ☐ approved by the examiner; ☐ disapproved by the examiner (see explanation).
11. ☐ The proposed drawing correction, filed _____, has been ☐ approved; ☐ disapproved (see explanation).
12. ☐ Acknowledgement is made of the claim for priority under U.S.C. 119. The certified copy has ☐ been received ☐ not been received ☐ been filed in parent application, serial no. _____; filed on _____.
13. ☐ Since this application appears to be in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under Ex parte Quayle, 1935 C.D. 11; 453 O.G. 213.
14. ☐ Other

EXAMINER'S ACTION

Claims 4-7, 9-17, 19, and 23-26 are rejected under 35 U.S.C. § 112, first paragraph, as the disclosure is enabling only for claims limited to methods of producing an alkalophilic asporogenic Bacillus novo species PB92 of minimal indigenous extracellular protease level, transformed with a mutated B. novo PB92 alkaline protease. See M.P.E.P. §§ 706.03(n) and 706.03(z).

The claims are not properly enabled for the recitation of the phrase "mutant high alkaline protease", and claim 17 is also not enabled for such proteases "differing in at least one amino acid from a wild-type high alkaline protease". Applicants arguments have been considered but are not deemed persuasive. Applicants state that "it would be well within the skill of one of ordinary skill in the art to determine which mutations would result in a protease differing by at least one amino acid from the indigenous protease". This is not deemed persuasive, as again, one of ordinary skill in the art would not be able to determine what type of mutation, how many, at what amino acid, etc., including all variations possible in order to fulfill what the applicants truly regard as the invention. Further, one skilled in the art could not prophetically predict the outcome of any mutation upon the gene, the enzyme produced, and their resultant effect upon the instantly claimed invention.

The following is a quotation of 35 U.S.C. § 103 which forms the basis for all obviousness rejections set forth in this Office action:

> A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.
>
> Subject matter developed by another person, which qualifies as prior art only under subsection (f) or (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.

Claims 4-17, 19, and 23-26 are rejected under 35 U.S.C. § 103 as being unpatentable over Fahnestock et al. and Estell et al., in view of TeNijenhuis and Suggs et al. The references and rejection are herein incorporated as cited in a previous Office Action.

Applicant's arguments filed in paper # 13 have been fully considered but they are not deemed to be persuasive. Applicants state that Fahnestock et al. and Estell et al. would not lead one to the instant invention in light of the secondary references. Applicants assert that the prior art differs, as for example, since Fahnstock et al. inserts a CAT fragment into the protease sequence, there is the possibility of reversion. This is not found persuasive for the reasons of record. Fahnstock et al. use homologous recombination to delete the original functional gene, as do applicants. Estell et al. compliment this by a similar deletion, with the replaced flanking regions containing only a

small portion of the original coding region of the protease. It would have been obvious to further delete the rest of the coding region, for the mere assurance of complete success of no protease activity. Estell et al. have shown that this method produces no (neutral) protease activity, and applicants method does not differ patentably from this by deleting the rest of the coding region. Applicants have not demonstrated any results that would have been unexpected, unobvious, or superior to that taught by the prior art, absent convincing evidence to the contrary.

Again, the limitation of "an alkalophilic Bacillus strain" does not render the claim patentably distinct from the similar methods of Fahnestock et al. and Estell et al., per se. The systems are the same, and both used with Bacillus organisms, of which many are already alkalophilic. Further, the mutation of the strain to produce an "asporogenic" variant is obvious and well known in the art to do, and is easily obtained via classic UV mutation techniques. Thus, the claims are not deemed patentable in view of the prior art.

NO CLAIM IS ALLOWED.

**THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 C.F.R. § 1.136(a).

A SHORTENED STATUTORY PERIOD FOR RESPONSE TO THIS FINAL ACTION IS SET TO EXPIRE THREE MONTHS FROM THE DATE OF THIS ACTION. IN THE EVENT A FIRST RESPONSE IS FILED WITHIN TWO MONTHS OF THE MAILING DATE OF THIS FINAL ACTION AND THE ADVISORY ACTION IS NOT MAILED UNTIL AFTER THE END OF THE THREE-MONTH SHORTENED STATUTORY PERIOD, THEN THE SHORTENED STATUTORY PERIOD WILL EXPIRE ON THE DATE THE ADVISORY ACTION IS MAILED, AND ANY EXTENSION FEE PURSUANT TO 37 C.F.R. § 1.136(a) WILL BE CALCULATED FROM THE MAILING DATE OF THE ADVISORY ACTION. IN NO EVENT WILL THE STATUTORY PERIOD FOR RESPONSE EXPIRE LATER THAN SIX MONTHS FROM THE DATE OF THIS FINAL ACTION.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Keith Hendricks whose telephone number is (703) 308-2959.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

ROBERT A. WAX
SUPERVISORY PATENT EXAMINER
GROUP 180

kdH
February 26, 1993